

THE TOLERANCE OF ANIMALS TO ACUTE HYPOXIA AFTER CONDITIONING TO PHYSICAL LOADS UNDER HIGH-ALTITUDE CONDITIONS

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ABSTRACT: This research has been conducted on white mice and rats. The mice were conditioned to both static (hanging on poles) and dynamic (running on a treadmill) work, the rats only to dynamic. The conditioning was carried out under middle-altitude conditions (altitude of 2000 m). The changes in weight of the animals, number of erythrocytes, the amount of hemoglobin, the oxygen requirements and the lifetime at altitudes of 9000 - 12,000 m were determined. It was found that conditioning to dynamic work under middle-altitude conditions slightly increases the tolerance of rats of acute hypoxia: such conditioning to static loads under these same conditions does not affect the tolerance of the organism to acute hypoxia.

The question as to the mutual influence of conditioning to physical loads and adaptation to high-altitude conditions has great practical significance and is of definite theoretical interest. The practical significance of the question is concerned, on the one hand, with the fact that for physiologists of sport it is important to explain the influence on athletic accomplishments of the repeated use of physical exercises under conditions of a slight oxygen deficiency in the inhaled air; on the other hand, for aviation and space medicine, it is necessary to solve the problem of including physical loads in the schedule of adaptation to hypoxic hypoxia. /85

Conditioning to muscular activity, in the opinion of the majority of investigators, in itself causes an increase in the tolerance to different adverse factors including acute hypoxia [3,4,11,12]. N.V. Zimkin, M.M. Bogorad, L.P. Zimnitskaya and others feel that the nonspecific effect on an organism of physical exercise has no less importance than does the specific effect of one or another factor [9].

Without denying the fact that, with an increase in tolerance to one of the irritants, the reaction of the organism is changed to some degree to the effect of the others, M.Ye. Marshak and his associates emphasize the great significance of the principle of "nonspecificity" in the development of the process of adaptation [15,17].

The physiological mechanisms of conditioning to physical loads to some degree is similar to the restructuring of the organism in the process of adaptation to hypoxia. With intense muscular activity, just as with hypoxic hypoxia, there is developed in man a hypoxemia due to the noncorrespondence between the transport and the requirements of oxygen [13,14,16]. In this respect we can expect positive results from the cumulation of changes produced by conditioning to physical loads and adaptation to hypoxia. However, it should be borne in mind that along with the overall changes in the functional state with physical conditioning and adaptation to hypoxia there are also substantial differences produced in first order by important factors such as CO₂. One characteristic of the adaptation to hypoxemia during motive activity is the simultaneous adaptation to hypercapnia, whereas with adaptation to hypoxic hypoxia an adaptation to hypocapnia is developed. Therefore, the adaptation mechanisms in both cases may have substantial differences.

Experimental work on the problem of the mutual influence of muscular conditioning and adaptation to hypoxia may be divided into three groups.

The first group of investigations carried out with athletes was devoted to the influence of preliminary adaptation to hypoxia under high-altitude conditions on the subsequent activity of these or other physical exercises. A.P. Frolov, D.A. Alipov and others note a positive character of such an influence on the increase in athletic accomplishments [2,22].

The second group contains those investigations which were carried out mainly on animals in which a positive effect was shown of conditioning to muscular exercises on the tolerance to acute hypoxia [5,6,10,23].

In the third group of investigations, data are cited on the cumulation of changes during physical conditioning under hypoxic conditions [20,25]. P.K. Stoyanov studied changes in the EKG, blood pressure and vital capacity of the lungs in humans, both those who were involved with physical labor at high altitude and those who were not. The data obtained indicate that there is a difference in the functional changes in these two groups of subjects: in those who were engaged in physical labor the author observed a significant increase in the pulse rate, the arterial pressure, and an insignificant decrease in the vital capacity of the lungs at the beginning of residence at an altitude of 2925 m. In proportion to the adaptation, changes in the blood pressure gradually returned to the original level - the pulse became slightly more frequent even and the vital capacity of the lungs was greater than the original values. In persons who were not involved in physical labor, from the moment of arrival at high altitude and for the period of the entire six months of observation the pulse rate and the arterial pressure had a tendency to increase, and the

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vital capacity to decrease.

In the work of Clark et al there is some indication that in rats conditioned on a treadmill under hypoxic conditions the myoglobin increased by 50% in comparison with the animals who were conditioned under ordinary conditions [25].

By analyzing the literature data we come to the conclusion that apparently there is developed a certain cumulation of changes associated with conditioning to physical loads and adaptation of the organism to hypoxia. The nature of this phenomenon is quite complicated and its rules have been studied insufficiently. We can only assume that the cumulation includes changes which occur at various levels of regulation of the organism.

The present work is a part of the investigations whose purpose is to explain, on the one hand, the most optimal conditions for summation of the changes which occur as a result of the physical conditioning and adaptation to hypoxia and, on the other hand, to attempt a study of the mechanisms which form the basis of this summation.

In this report we give results of investigations in which we compare the influence of conditioning to static and dynamic loads under high-altitude conditions on the adaptation effect determined basically from the tolerance of animals to acute hypoxia.

The work was carried out on 180 white mice and 45 white rats. The mice were divided into 6 groups, with thirty in each:

Group 1: Control, Moscow;

Group 2: Mice, subjected for 33 days to high-altitude conditions at an altitude of 2000 m above sea level;

Group 3: Mice, conditioned to static loads at an altitude of 2000 m;

Group 4: Mice, conditioned to dynamic work at an altitude of 2000 m;

Group 5: Animals subjected to an altitude of 2000 m for 14 days and to an altitude of 3800 m for 19 days;

Group 6: Mice, conditioned to static loads at altitudes of 2000 and 3800 m.

The rats were divided into three groups:

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Group 1: Control;

Group 2: Animals subjected for 33 days to an altitude of

2000 m.

Group 3: Rats conditioned to dynamic work at an altitude of 2000 m.

Conditioning to static and dynamic loads was carried out every other day, beginning from the 6 - 8th day of residence at high altitudes. For conditioning of the mice to static loads we used vertical poles. The animals were constrained on them for the first two days without load. From the third day a load of 10 g was suspended from the tail of the animal (the weight of the mouse was from 16 - 18 g). The load was gradually increased as the time the animal remained on the pole was increased. The first three tests of the mouse was for 5 minutes. From the fourth test this time was extended by 1.5 minutes with each test. In all 13 conditioning periods were made.

To condition the mice and rats to dynamic work we constructed a special treadmill. The rate at which the animals ran was maintained constant: 24 m per minute for the mice and 36 m for the rats. The conditioning to dynamic loads for the rats was begun with a path of 120 m. This load was maximal for the rats. We included in our problem carrying out conditioning to loads of average intensity, therefore from the third test the length of the path was decreased to 36 m. The conditioning of the mice was begun from 24 m.

The load for the rats was increased with each conditioning test by increasing the length of the path by 6 m (14 tests in all). In the mice such an increase in load occurred only in the first four tests after which until the end the load remained constant (13 conditioning tests).

In all groups of animals regularly during their residence under high-altitude conditions and upon return to Moscow we studied the changes in the amount of hemoglobin, the number of erythrocytes, the reticulocytes and eosinophils (the blood was taken from an incision at the end of the tail), we studied the oxygen requirement after Kolabukhov. In the conditioned animals the oxygen requirement was determined both before and after the load for the 5th - 15th minute of the recovery period every minute, then every 20 - 30 minutes, 40 - 50 minutes, 60 - 70 minutes and after three hours. Upon return to Moscow in all three groups of animals we determined the lifetime under conditions of ascent in a pressure chamber. The mice were raised at a rate of 75 - 80 m/sec to altitudes of 9000 m. At this altitude the first 10-minute rest was taken. Another 10-minute rest was given after each 1000 m. The rats were raised to 11,000 m. The first rest was for 10 minutes, then each 5 minutes every 1000 m. The condition of the animals and the dynamics of their death were fixed as a function of the "altitude" and time of residence.

Residence of the rats at an altitude of 2000 m led to a slight /88 increase in the erythrocytes and did not change the amount of hemoglobin.

Changes in the red blood in the mice differed from the changes in the rats. In the mice the number of erythrocytes increased gradually. In comparison with the group of animals who remained in Moscow, their increase was 15%. The amount of hemoglobin for the entire extent of residence in the mountains varied in a wave shape: during the first eight days there was observed a drop in the hemoglobin on the average from 15 to 11 g%; by the 18-24th day the amount of hemoglobin increased to 18 g% and then again decreased insignificantly by the end of the expedition.

The first days of residence in the mountains were accompanied by a significant drop in the number of eosinophils both in the mice and in the rats by an increase in the number of reticulocytes. From the 8 - 10th day the number of eosinophils in the peripheral blood began to increase gradually and by the end of residence exceeded the original values by approximately 3 times. The number of reticulocytes on the contrary decreased slightly (Table 1).

TABLE 1. CHANGES IN THE NUMBER OF RETICULOCYTES AND EOSINOPHILS IN RATS AND MICE IN THE PROCESS OF ADAPTATION TO HYPOXIA AT AN ALTITUDE OF 2000 m (AVERAGE VALUES).

Animals	n	Number of eosinophils per 1 cm ³							Number of reticulocytes by 1000					
		Before Adaptation	During Adap- tation, days				After Adap- tation, days			Before Adaptation	During Adap- tation, days			After Adaptation
			3-4	9	18-19	33	3	11	20		3-4	9	18-19	
Rats	8	98	17	—	95	349	110	—	—	22	190	—	88	14
Mice	10-15	102	22	61	—	288	81	85	65	—	—	44	32	30

The effect of dynamic loads and conditioning to them produced changes in the red blood in the rats and the mice.

In the rats, after carrying out the first two tests, there was observed a decrease in the number of erythrocytes by 25%, on the background of increase in hemoglobin by 25% in comparison with the unconditioned animals. By the end of the cycle in both groups of animals the number of erythrocytes and the amount of hemoglobin were equal (Fig. 1).

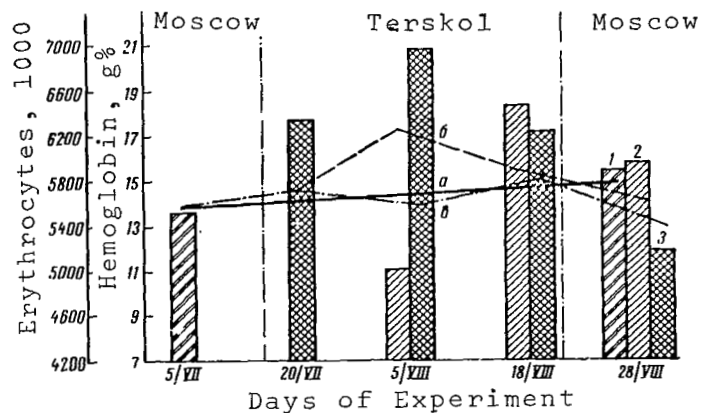


Fig. 1. Effect of Conditioning to Dynamic Work Under Middle-Altitude Conditions on the Number of Erythrocytes and the Amount of Hemoglobin in Rats. Erythrocytes: 1. Control; 2. In Animals with Dynamic Load; 3. Intact. Hemoglobin: a. Control; b. In Animals with Dynamic Load; c. Intact.

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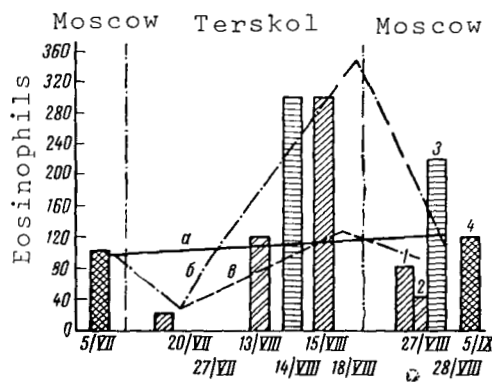


Fig. 2. Effect of Conditioning to Dynamic and Static Loads under Medium-Altitude Conditions on the Amount of Eosinophils in the Peripheral Blood. Mice: 1. Intact; 2. With Dynamic Load; 3. With Static Load; 4. Control. Rats: a. Control; b. Intact; c. With Dynamic Load.

In the mice the conditioning to dynamic loads produced the same increase in the number of erythrocytes as in the passively adapted animals. In the conditioned mice the amount of hemoglobin gradually and insignificantly decreased. As shown above, in the passively adapted animals no drop in hemoglobin was observed, and its changes had an expressed wave-shape character.

Both in the mice and in the rats conditioned to dynamic load, unlike those who were only adapted, no eosinophilia was noted - the number of eosinophils did not exceed the values which are characteristic for Moscow (Fig. 2). This effect is worthy of attention. The eosinophilia observed under high-altitude conditions was assumed by several of the investigators to be a symptom which indicates a functional exhaustion of the adrenal glands. The lack of eosinophilia in animals who underwent conditioning to dynamic work under high-altitude conditions contradicts this point of view. The reaction of the reticulocytes in conditioned mice and rats did not differ from the reaction in the unadapted animals.

The decrease in the number of erythrocytes in rats expressed at the beginning of conditioning was associated apparently with deepening of the hypoxic state under the influence of extreme muscular load (the first two tests with maximal load). We may assume that the accumulation in the blood of incompletely oxidized products of decomposition leads to an acceleration of destruction of the erythrocytes. A further increase in the number of erythrocytes indicates a correct choice of the intensity of conditioning schedule and its positive influence on the organism. Our data agree with the results obtained by G.A. Goryanaya [8].

Change in the weight of the conditioned and unconditioned rats at an altitude of 2000 m confirms this assumption. The weight of both groups varied approximately the same. Here the weight of the animals adapted to mountainous conditions, lagged from the weight of the control group who remained in Moscow (the weight of the adapted animals was 243 g, those passively adapted to hypoxia was 235 and the control animals was 260 g).

Only the mice were adapted to static loads. This conditioning was not manifested in the changes in the studied blood characteristics. The amount of hemoglobin, number of erythrocytes and eosinophils in the conditioned mice was the same as in the unconditioned animals.

Thus the reaction of the red blood and the eosinophils to conditioning to dynamic work differed from the reaction to conditioning to static loads.

Residence at high altitude led to a slight increase in the oxygen requirements of the animals in comparison with the control group. In the mountains, for the animals who were adapted to dynamic work, there was the greatest oxygen requirement. Upon

return to Moscow the oxygen requirement of this group of animals was the least. The group of animals conditioned to static loads did not differ in oxygen requirements from the group of unconditioned animals.

These data indicate that conditioning of animals to dynamic work under high altitude conditions was reflected by the degree, /91 and in several instances also by the character, of the physiological changes which occur in the process of conditioning. Conditioning to static loads was not accompanied by any peculiar characteristics.

As was shown above, after return to Moscow for all groups of animals, we investigated the tolerance to acute hypoxia.

Residence at an altitude of 2000 m without conditioning not only did not give an increase in tolerance to acute hypoxia but also produced even a slight statistically unreliable decrease.

The rats who were adapted to dynamic work under high-altitude conditions increased their tolerance to acute hypoxia (Table 2).

TABLE 2. LIFETIME OF DIFFERENT GROUPS OF RATS UNDER CONDITIONS OF ACUTE HYPOXIA (11,000 - 13,000 m)

Group	After Completion of Adaptation			
	Third day		12th day	
	Lifetime, min	P	Lifetime, min	P
Control, Moscow	11.3	< 0.5	7.8	> 0.5
Adaptated, 2000 m	9.7	> 0.01	5	< 0.5
Conditioned at 2000 m	15.8	< 0.5	9	> 0.5
Control, Moscow	11.3		7.8	

In the mice on the third day following completion of the conditioning and adaptation we did not observe any higher tolerance in comparison to the passively conditioned animals. The differences in the altitude tolerance between the animals subjected to an altitude of 3800 m (Ledovaya Baza) and the mice subjected at this altitude to conditioning to static loads, were statistically unreliable. The effect on tolerance to acute hypoxia of adaptation at different altitudes is clearly shown in Table 3.

On the 28th day the mice who were conditioned to dynamic loads, unlike the other groups of animals, still retained an increased tolerance to acute hypoxia ($P > 0.01$).

The lack of any influence from conditioning to static loads on the tolerance to acute hypoxia is associated apparently with

the fact that in itself the static loads do not produce any increase in the hypoxic state: saturation of blood with oxygen, as a rule, in carrying out static loads, does not change or changes incomparably to a lesser degree than with dynamic work [5-7]. Omission of the hypoxemic factor which is basic and common for the oxygen deficiency and the physical loads, probably is explained by the absence of a "nonspecific" influence of conditioning to static loads on the tolerance to acute hypoxia. /92

TABLE 3. LIFETIME OF MICE AT AN ALTITUDE OF 9000 - 12,000 m (AVERAGE VALUES FOR 9 - 10 ANIMALS).

Group	After Completion of Adaptation			
	4th day		28th day	
	Lifetime	P	Lifetime	P
3800 m, unconditioned	24 min 35 sec	< 0.5	2 min 53 sec	< 0.5
3800 m, "static"	28 " 20 "	> 0.1	2 " 31 "	< 0.5
2000 m, unconditioned	16 " 42 "	< 0.5	2 " 02 "	< 0.5
2000 m, "static"	11 " 07 "	< 0.5	1 " 42 "	> 0.01
2000 m, "dynamic"	11 " 44 "	> 0.01	6 " 47 "	> 0.01
Intact, Moscow	3 " 28 "		1 " 45 "	

Thus, conditioning to dynamic work under high-altitude conditions somewhat increases the tolerance of the rats to acute hypoxia; conditioning to static loads in the schedule which we chose under high-altitude conditions does not influence the tolerance of the organism to acute hypoxia.

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